

Claims:

1. A method for estimating the disease risk of an individual comprising

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- establishing a sample from said individual,
- assessing in the genetic material in said sample a sequence polymorphism

10 - in a region corresponding to SEQ ID NO: 2, or a part thereof, or

- in a region complementary to SEQ ID NO: 2, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof,

15 - obtaining a sequence polymorphism response,

- estimating the disease risk of said individual based on the sequence polymorphism response.

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2. The method according to claim 1, wherein a sequence polymorphism is assessed

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- in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- in a region complementary to SEQ ID NO: 1, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof.

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3. The method according to claim 1, wherein the cell sample is a blood sample, a tissue sample, a sample of secretion, semen, ovum; a washing of a body surface, such as a buccal swap, a clipping of a body surface, including hairs and nails.

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4. The method according to any of the preceding claims, wherein the cell is selected from white blood cells and tumor tissue.
5. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one mutation base change.
6. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two base changes.
10. 7. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one single nucleotide polymorphism.
8. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two single nucleotide polymorphisms.
15. 9. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one tandem repeat polymorphism.
20. 10. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two tandem repeat polymorphisms.
25. 11. The method according to any of the preceding claims, wherein the cancer is selected from skin carcinoma including malignant melanoma, breast cancer, lung cancer, colon cancer and other cancers in the gastro-intestinal tract, prostate cancer, lymphoma, leukemia, pancreas cancer, head and neck cancer, ovary cancer and other gynecological cancers.
30. 12. The method according to any of the preceding claims, wherein the cancer is selected from skin cancer, lung cancer, colon cancer and breast cancer.
35. 13. The method according to any of the preceding claims, wherein the cancer is selected from skin cancer and breast cancer.
14. The method according to any of the preceding claims 11-13, wherein the skin cancer is basal cell carcinoma.

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15. The method according to any of the preceding claims, wherein the assessment
is conducted by means of at least one nucleic acid primer or probe, such as a
primer or probe of DNA, RNA or a nucleic acid analogue such as peptide nucleic
acid (PNA) or locked nucleic acid (LNA).

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16. The method according to claim 15, wherein the nucleotide primer or probe is
capable of hybridising to a subsequence of the region corresponding to SEQ ID
NO: 1; or a part thereof, or a region complementary to SEQ ID NO:1.

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17. The method according to claim 15, wherein the primer or probe has a length of
at least 9 nucleotide or peptide monomers.

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18. The method according to any of the preceding claims 15-17, wherein at least
one primer or probe is capable of hybridising to a subsequence selected from
the group of subsequences

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1. GCTCTGAAAC TTACTAGCCC(A/G)GTATTTATGG AGAGGCATT
2. GTGGTCAAAT TCTCATT CAT CGTGG (T/C) CCAGGCAAGC
ACACTTCCTC

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3. ACCCTGAGGT GAGCACCTGT TCCTT(C/T) TCCTTGCCCT TAGCCA-
GAG GTAGA

4. GGGCAGGGGT TTGTGCCTCC AATGA (G/A) CACAAGCTCC
CCCTGCCCTT CAACT

5. CCTGGCGGTG GCCGTACCA GCTTT (T/C) GGGGGTGT
GGGAAGCTGG

6. CTCCAGCCCC ACTGTTCCCT (A/G) GGCCCTATTG GTCCCCCTGG

7. ACAAGGAGGA GGCAGAAGTG AGGTT (G/C) AAACCCACTG CCCAATC-
TTA

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8. CCAACACGGT GAAACCCGT CTGTA(T/C) TAAAAATACA AAAATTAGCC

9. AATCCAGGAC CCCATAATCT TCCGT (C/T) ATCTAAAACA ATA-
ATGGTGA

10. CCCAAGGGGG CGAGGGGAGG GTGAA (A/G) GGGTGGGACG
GGGGCAGCCG

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11. GAAGTGAGAA GGGGGCTGGG GGTGCG (G/-) CGCTCGCTAG
CGGGCGCGGG
12. CGCACGCGCA GTATCCCGAT TGGCT (C/G) TGCCCTAGCG GATT-
GACGGG
- 5 13. AACTCCTGGG TTGATCAAT ACTCA (GACA/-) ATCTTGGCAG
GCGCAGGAGG
14. GCTGGGATTA CAGGCTTGAG CCACC (A/G) CGCCCGGCCT
GCAAAGCCAT
15. TTTTGTATCT TTAGTAGAGA CAGG (T/G) TTTCTCCATG TTGGTCAGGC
- 10 16. GCCTCAGCCT CCCGAGTAGC TGAGACT (C/A) CAGGTGCCCG CCAC-
CACGCC
17. TGAAATTGTA GGTTGAGAGG CCAGGCG (C/T) GGTGCTCACG
CCTGTAATT
18. GTTTATAAAC ATAAACCCAG (T/A) GCTGTGTGAA GGCACCTAAT
- 15 19. CCGTCTCTAT TAAAAATATA AAA (A/C) ATTAGCCG GGTGTAGCGG
20. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT
21. TCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC
22. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCCT CCAGCCTGGG
23. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC
- 20 24. CTGGGTTCTA GAACTACC (C/T) ATGCAAACCC AGCTGTTCC
25. ATTCTGCCCT GGTTCTAGA ACTACCT (C/A) TGCAAACCCA
GCTGTTCCC
26. GCTGTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
CACCTCCGCC
- 25 27. GACCTAGAAG ATGGTCGAG A (C/T) AGCAGCTTGA GGCTGGCAGG
28. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
ACCGTCTCGC
29. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCTGA AAGTCATCGA
30. GCAGCCCCGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG
31. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTCT CCCCCCTGCTT
32. ACAGGAGAGG GAAGGTTTTTG (A/T) TTTTTTTTTT GTTTTTTTT
33. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAACCTTC GAGCCA-
GAAG
34. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
CAGCT

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35. TTGAGACTCT CTGTTGAT (A/G) CTTCACTCAG AAGGTGCTTC
36. AGGCCAGGCT CCTGCTGGCT G (C/G) GCTGGTGCAG TCTCTGGGA
37. CCCCTATACC CTCAAGCAT (C/T) TATCCATTGA GTTACAAACA
38. ACCATCCCCC GCCTTCCGTT (A/C) GTCCGGCCCC CGAGGCTAGC

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or to a sequence complementary to any of the subsequences.

19. The method according to claim 18, wherein at least one nucleotide probe is selected from the group consisting of

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1. TGAAATTGTA GGTTGAGAGG CCAGGCG (C/T) GGTGCTCACG
CCTGTAATT
2. GTTTATAAAC ATTAAACCAG (T/A) GCTGTGTGAA GGCACTTAAT
3. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTAGCCG GGTGTAGCGG
4. GGGAGGCTCG AGGCAGGGC (A/G) GATTGCATGA GCTCAGGATT
5. TCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATT
6. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG
7. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC
8. CTGGGTTCTA GAACTACC (C/T) ATGCAAACCC AGCTGTTCC
9. ATTCTGCCCT GGGTTCTAGA ACTACCT (C/A) TGCAAACCCA
GCTGTTCCC
10. GCTGTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
CACCTCCGCC
11. GACCTAGAAC ATCGGTCGAG A (C/T) AGCAGCTTGA GGCTGGCAGG
12. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
ACCGTCTCGC
13. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCTGA AAGTCATCGA
14. GCAGCCCGGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG
15. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTTCT CCCCCCTGCTT
- 30 16. ACAGGAGAGG GAAGGTTTTTG (A/T) TTTTTTTTTT GTTTTTTTT
17. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAAACCTTC GAGCCA-
GAAG
18. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
CAGCT

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or to a sequence complementary to any of the subsequences.

20. The method according to claim 19, wherein at least one nucleotide probe is selected from the group consisting of

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1. GTTTATAAAC ATAAACCAG (T/A) GCTGTGTGAA GGCACCTTAAT
2. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTAGCCG GGTGTAGCGG
3. GGGAGGCTCG AGGCCGGC (A/G) GATTGCATGA GCTCAGGATT
4. TCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC
5. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG

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or to a sequence complementary to any of the subsequences.

21. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 1521-37752 (r).

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22. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 7760-22885 (RAI).

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23. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 34391- 37752.

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24. The method according to any of the preceding claims, wherein at least two different probes are used, one probe being selected from the probes as defined in any of claims 17-21, and the other probe being capable of hybridising to a sequence different from SEQ ID NO: 1, or a part thereof, or to a sequence complementary to a region different from SEQ ID NO: 1, or a part thereof.,

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25. The method according to claim 1, wherein the translational product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, is an antibody, such as a monoclonal or polyclonal antibody.

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26. A method for estimating the disease prognosis of an individual comprising

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- providing a sample from said individual,
- assessing in the genetic material in said sample a sequence polymorphism

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- in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- in a region complementary to SEQ ID NO: 2, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof,

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- obtaining a sequence polymorphism response,
- estimating the disease prognosis of said individual based on the sequence polymorphism response.

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27. The method according to claim 26, wherein the method has any of the features as defined in any of the claims 2-25.

20 28. A method for estimating a treatment response of an individual suffering from cancer to a disease treatment, comprising

- providing a sample from said individual,
- assessing in the genetic material in said sample a sequence polymorphism

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- in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- in a region complementary to SEQ ID NO: 1, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof,

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- obtaining a sequence polymorphism response,
- estimating the individual's response to the disease treatment based on the

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sequence polymorphism response.

29. The method according to claim 28, wherein the method has any of the features
as defined in any of the claims 2-25.

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30. A primer or probe for use in a method as defined in any of the claims above,
said primer or probe being selected from

TGGCTAACACCGTGAAACC(SEQ ID NO:7)

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GGAATCCAAGATTCTATGATGG(SEQ ID NO:8)

GGGAGGCAGGAGCTTGCAGTGA (SEQ ID NO:9)

CTGAGATCGCACCACTGCAC (SEQ ID NO:10)

GGTTTTCTGCTCTGCACACG (SEQ ID NO:11)

CCTTTCTCCTCCACCAACG (SEQ ID NO:12)

15

CGGGCTACAGGGTTACCTGAG (SEQ ID NO:13)

TCTGCAACCTGGTGCGAGCAGC (SEQ ID NO:14)

CCTACCACCATCATCACATCC (SEQ ID NO:15)

GCCTTGCCAAAAATCATACC (SEQ ID NO:16)

CCTCTCCCCAATTAAGTGCCCTCACACAGC (SEQ ID NO:17)

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AGCCAGGGAGGTTGAGGCT (SEQ ID NO:18)

AGACAGCCCCTGAATCAGGCAC (SEQ ID NO:19)

GCAATGAGCCGAGATAGAA (SEQ ID NO:20)

TGGCTAGCCCATTACTCTA (SEQ ID NO:21)

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31. A primer or probe for use in a method as defined in any of the claims above as
the other probe

GCCCCGTCCCAGGTA (SEQ ID NO:74)

AGCCCCAAGACCCCTTCACT (SEQ ID NO:22)

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GTCCCATAGATAGGAGTGAAAG (SEQ ID NO:23)

CCCTAGGACACAGGAGCACA (SEQ ID NO:24)

TTGTGCTTCTGTGTCCA (SEQ ID NO:25)

TATCAGAAAAGGCTGGAGGA (SEQ ID NO:26)

GAGTGGCTGGGGAGTAGGA (SEQ ID NO:27)

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GCCAAGCAGAAGAGACAAA (SEQ ID NO:28)

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CCTCAGATGTCCCTGCTCA (SEQ ID NO:29)
GCCACAGCCCCAGCAAGTAG (SEQ ID NO:30)
AGGACACCAGGACACGCAGA (SEQ ID NO:31)
CATAGAACAGTCCAGAACAC (SEQ ID NO:32)
5 TTAGCTTGGCACGGCTGCCAAGGA (SEQ ID NO:33)
ACAGAATTGCCCGGCCTGGTACAC (SEQ ID NO:34)
TTGAAACTGGAACTCTGAGAAGG (SEQ ID NO:35)
TGGTGGATGGTGTGAAGCA (SEQ ID NO:36)
CCTTCCTCCAACCTCTCCATTCCACC (SEQ ID NO:37)
10 GGGGATCATGTCGTAATGGACT (SEQ ID NO:38)
ATGCCCTGTAGGTTCAATGG (SEQ ID NO:39)
TGGAGGTCTTAGGGGCTTG (SEQ ID NO:40)
GGCTGGTCCCCGTCTCTCCTTCC (SEQ ID NO:41)
TCTCTGTTGCCACTTCAGCCTC (SEQ ID NO:42)
15 GTCCTGCCCTCAGCAAAGAGAA (SEQ ID NO:43)
TTCTCCTGCGATTAAAGGCTGT (SEQ ID NO:44)
ATCCTGTCCTACTGGCCATT (SEQ ID NO:45)
TGTGGACGTGACAGTGAGAAAT (SEQ ID NO:46)
TGGAGTGCTATGGCAGGATCTCT (SEQ ID NO:47)
20 CCATGGGCATCAAATTCTGGGA (SEQ ID NO:48)
CACACCTGGCTCATTGTAT (SEQ ID NO:49)
TCATCCAGGTTGTAGATGCCA (SEQ ID NO:50)
AGGCTCAACAAGGAAAAATGC (SEQ ID NO:51)
GCTAGACAGTCAGGGAGGGACG (SEQ ID NO:52)
25 AAAGGGTGGGTGTGGGAGACATTGG (SEQ ID NO:53)
AAACCAACCTAGGCACCCCCAAA (SEQ ID NO:54)
CAGTGTCCAAGAGCACC (SEQ ID NO:55)
CTACCCCTTAGCGACC (SEQ ID NO:56)
TCCTGCCCTCAGAGCGTCACC (SEQ ID NO:57)
30 GTACGGTCCACATAATTGGAGGA (SEQ ID NO:58)
CGACGAACCTCTCTGAAGCGAA (SEQ ID NO:59)
AGCGACACGGGCATCTGG (SEQ ID NO:60)
ATGAGCGTCCACCTCCTGAACC (SEQ ID NO:61)
AGGCAGCAGCATCGTCATCCCC (SEQ ID NO:62)
35 TGCATAGCTAGGTCCCTGC (SEQ ID NO:63)

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AACTGACRAAACTAGCTCTATGGGTGGTGCCGCA (SEQ ID NO:64)

CTGGCTCTGAAACTTACTAGCCC (SEQ ID NO:65)

GCTGGACTGTACCGCATG (SEQ ID NO:66)

GGAGCAGGGTTGGCGTG (SEQ ID NO:67)

5 TGCCCTCCCAGAGGTAGGCCCT (SEQ ID NO:68)

CCCTCCCGGAGGTAAGGCCTC (SEQ ID NO:69)

GATCAAAGAGACAGACGAGO (SEQ ID NO:70)

GAAGCCCAGGAAATGC (SEQ ID NO:71)

GGACGCCAACCTGGCCAACC (SEQ ID NO:72)

10 CGTGCTGCCAACGAAAGTG (SEQ ID NO:73)

32. The primer or probe according to any of claims 29, 30 or 31, wherein the probe is operably linked to at least one label, such as operably linked to two different labels.

15 33. The probe according to claim 31, wherein the label is selected from TEX, TET, TAM, ROX, R6G, ORG, HEX, FLU, FAM, DABSYL, Cy7, Cy5, Cy3, BOFL, BOF, BO-X, BO-TRX, BO-TMR, JOE, 6JOE, VIC, 6FAM, LCRed640, LCRed705, TAMRA, Biotin, Digoxigenin, DuO-family, Daq-family.

20 34. The primer or probe according to any of claims 29-32, wherein the primer or probe is operably linked to a surface.

25 35. The primer or probe according to claim 33, wherein the surface is the surface of microbeads or a DNA chip.

36. An antibody directed to an epitope of a RAI gene product.

30 37. A kit for use in a method as defined in any of the claims above, comprising at least one primer or probe, said probe being as defined in any of claims 30-36, and optionally further amplifying means for nucleic acid amplification.

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